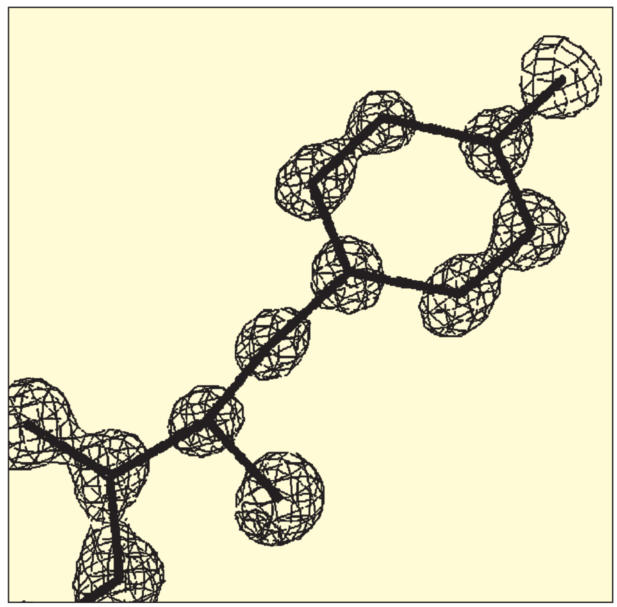
STS-95

Understanding the Biochemistry of Disease Through Protein Crystal Growth

Proteins are involved in nearly every one of the body's metabolic processes, including the onset of infection and disease. Several experiments aimed at increasing fundamental understanding of the biochemistry of proteins will fly on STS-95. Researchers will attempt to grow large, defect-free crystals of proteins in order to determine or reveal more details of the proteins' structures. Crystals grown in microgravity tend to be more highly ordered than those grown on Earth, making them easier to analyze for the determination of three-dimensional structure. Using such methods as X-ray diffraction, scientists can pinpoint the location of molecules in the protein crystal. That information can then be useful in the design of pharmaceuticals that can interact with a protein and alter its function.

PCAM cylinder, actuator plate, sample tray, sample holders, and flexible rubber membrane

The Protein Crystallization Apparatus for Microgravity (PCAM) will be used for growing protein crystals on STS-95. PCAM uses vapor diffusion to grow protein crystals. Vapor diffusion is a process in which the liquid in a protein solution is allowed to evaporate, thereby increasing protein concentration and triggering nucleation, or growth, of protein crystals. Each PCAM cylinder can



Computer-generated structural model of pike parvalbumin

hold nine stackable trays carrying seven individual protein samples per tray, allowing up to 63 protein experiments to be run in each cylinder. The Single-Locker Thermal Enclosure System accommodates six cylinders, for a total of 378 experiments in a single space shuttle locker. PCAM's high sample capacity and the ease with which samples can be prepared for flight and distributed postflight meet NASA's requirement for cost-effective research and satisfy a co-investigator's need for frequent flight experiments.

Candidate proteins for flight experiments in the PCAM are selected based on proposals submitted to the principal investigator and represent the work of an international group of scientists from industrial, academic, and government laboratories. Selection is based on theories that help identify proteins that are most likely to benefit from growth in microgravity and on external peer review. Several of the proposed proteins for flight on STS-95 have been flown before, yielding important results. Reflight on STS-95 will allow researchers to continue ultrahigh-resolution studies of protein structures and will provide more information needed to understand the physics of obtaining improved size and quality of protein crystals. A sampling of proteins that have flown previously follows:

Pike Parvalbumin

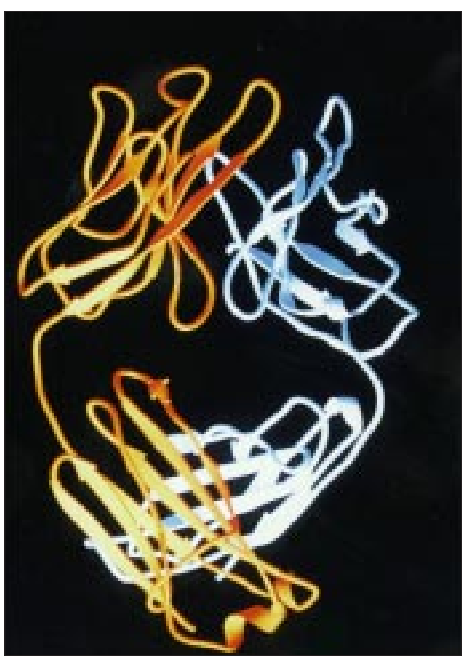
Co-investigator: Jean-Paul Declercq
University of Louvain, Belgium

Parvalbumins are proteins found in the muscles, endocrine glands, skin cells, and some neurons of vertebrates, but the role they play for musculature is not yet understood. Researchers are exploring theories of a correlation between parvalbumin concentration levels and the relaxation speed of mammalian muscles after contraction. An ultrahigh-resolution structure was achieved from samples grown on STS-83 in April 1997, and in July 1997, during STS-94, PCAM produced the largest crystals of pike parvalbumin grown to date.

Respiratory Syncytial Virus (RSV)

Investigator: Daniel Carter
New Century Pharmaceuticals, Inc.

RSV causes an infection that attacks respiratory airways and lungs. Each year nearly four million U.S. children ages 1 to 5 are infected. Approximately 100,000 of these children require hospitalization, and 4,000 die annually from the resulting infection. Crystals of the neutralizing antibody against RSV grown during the STS-85 mission in August 1997 were larger and of higher quality than those grown in previous studies.



Computer-generated structural model of RSV

Eco RI Endonuclease-DNA Complex

Co-investigator: John Rosenberg
University of Pittsburgh

Research on this complex protein is important for understanding how proteins recognize and target specific sequences of DNA. Eco RI endonuclease leaves a trail that scientists can follow that tells them to which specific DNA sites the protein has bound. Researchers hope to discover how proteins discriminate between different DNA sequences that are very similar. Crystals of eco RI produced during STS-85 enabled the first high-resolution structure of this protein.

Investigations of many other proteins and viruses are included in the candidate list for the PCAM flight on STS-95. These include experiments useful in the study of the fundamental biochemistry of proteins and investigations of the roles proteins and viruses play in basic biological processes, including the onset of infection and disease. This information is essential for the development of structure-based therapeutic drugs. Other research is focused on understanding and predicting the growth of protein crystals.

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